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Dirk van den Boom

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EXAMINER

WOOLWINE, SAMUEL C

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/723,365	Applicant(s) BOOM ET AL.	
	Examiner SAMUEL WOOLWINE	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 74-168 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 74-168 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03/13/2008;06/23/2008;08/29/2008</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status

Claims 74-168 are pending in the application. Claims 129-168 are new claims (the underlining in claim 129 appears inadvertent, since it is a new claim).

The objection to claim 124 made in the Office action mailed 02/29/2008 is withdrawn in view of Applicant's amendment.

The rejection of claims 74-83, 85-91, 94-102, 105, 113 and 113 under 35 U.S.C. 102(b) over Foote et al (WO 98/54571) made in the OA 02/29/2008 is withdrawn in view of Applicant's amendment reciting one specific cleavage, and the examiner's interpretation of that amendment (see *Claim Interpretation* below). Consequently, all rejections under 35 U.S.C. 103(a) based on Foote are also withdrawn. The rejections were based in part on the assertion that since Foote experimentally deduces the *actual* sequence, this inherently identified a "reduced set of candidate sequence variations". However, Foote's method required multiple different specific cleavages, as opposed to one specific cleavage.

The rejection of claims 106-108, 118-120 and 124-128 under 35 U.S.C. 112, 2nd paragraph, is withdrawn in view of Applicant's amendment.

New grounds of rejection are set forth under 35 U.S.C. 101 in light of the recent decision in *In re Bilski*, 88 USPQ2d 1385 (Fed. Cir. 2008). Additional new grounds of rejection under 35 U.S.C. 112 are set forth below. Consequently, this action is NON-FINAL.

Claim Interpretation

Applicant has amended claim 74 as a method for "determining the sequence in one or more sequence variations in a target nucleic acid". The examiner construes this to mean just what is says, i.e. determining the sequence of a variation, not just that a variation is present. Applicant has also amended claim 74 to recite "one specific cleavage", which the examiner construes as foreclosing any additional specific cleavage reactions. It is noted that dependent claim 91, for example, recites "wherein two or more specific cleavage agents are utilized to generate fragments". This is not necessarily inconsistent with the "one specific cleavage" recited in claim 74, so long as both agents are used together in the same reaction. For example, cleaving a target nucleic acid in a reaction comprising a C-specific agent and a G-specific agent would produce "one specific cleavage".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 74-108, 112-114, 124-128, 129-161, 165-168 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: scoring the candidate sequence variations. Claim 74, step (d) recites "identifying a reduced set of candidate sequence variations corresponding to the compomer witnesses, whereby the one or more sequence variations in the target nucleic acid are determined from the candidate sequence variations". Similarly, claims

Art Unit: 1637

124 and 129 recite determining the sequence variation(s) from the candidate sequence variations [the algorithms in these claims being used to generate the set of *candidate* sequence variations]. In other words, after the set of candidate sequence variations (i.e. the list of *possible* sequences) is generated, the *actual* sequence of the variation(s) is determined. There is a gap in the method; how does one go from this list of possible sequences to the actual sequence? The only means taught in the disclosure that the examiner found was through the step of scoring the candidate sequences (for example, figure 1; paragraph [0027] of published application: "The value of the scores...can then be used to determine the sequence variation candidate that corresponds to the actual target nucleic acid sequence."). This is in fact recited in dependent claims 109 and 162, and it is recommended to incorporate such limitations into the independent claims (74, 124, 129) to obviate the rejection.

It is further noted for Applicant's consideration that incorporation of the scoring step into claim 74 would also distinguish over the prior art of Foote (WO 98/54571) and Zabeau (WO 00/66771), making the amendment to claim 74, step (a) (limiting to one specific cleavage) unnecessary. Rescinding the "one" limitation would appear to offer broader scope encompassing more practical embodiments where more than one cleavage is used.

Claims 124-128 are rejected under 35 U.S.C. 112, second paragraph, on further grounds as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Art Unit: 1637

Claim 124 recites a method for "detecting one or more sequence variations in a target nucleic acid", but then recites "providing...whether modified nucleotides or amino acids are incorporated into all or part of the target sequence". This does not make sense, as nucleic acids do not comprise amino acids. Also, claim 124 has steps (a), (b) and (d), but no step (c). Appropriate correction is required.

Finally, the phrase "whether modified nucleotides or amino acids are incorporated into all or part of the target sequence" is vague and indefinite, since it cannot be determined if this means "*providing a description as to whether modified nucleotides...are incorporated...*", or simply as a parenthetical phrase meaning that the method encompasses target nucleic acid sequences regardless of whether or not there are modified nucleotides in the target.

Claims 125-128 depend from claim 124 and are rejected for the same reasons.

Claim 128 is rejected under 35 U.S.C. 112, second paragraph, on further grounds as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 128 recites "wherein the sufficiently small mass difference is the resolution of the mass measurement". There is no longer antecedent basis for this limitation in the claim, since parent claim 124 has been amended to delete any reference to "a sufficiently small mass difference".

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Art Unit: 1637

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 74-84, 100-139 and 155-168 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The CAFC has set forth that:

"...we believe our reliance on the Supreme Court's machine-or-transformation test as the applicable test for § 101 analyses of process claims is sound.

Nevertheless, we agree that future developments in technology and the sciences may present difficult challenges to the machine-or-transformation test, just as the widespread use of computers and the advent of the Internet has begun to challenge it in the past decade. Thus, we recognize that the Supreme Court may ultimately decide to alter or perhaps even set aside this test to accommodate emerging technologies. And we certainly do not rule out the possibility that this court may in the future refine or augment the test or how it is applied. At present, however, and certainly for the present case, we see no need for such a departure and reaffirm that the machine-or-transformation test, properly applied, is the governing test for determining patent eligibility of a process under § 101." *In re Bilski*, 88 USPQ2d 1385 (Fed. Cir. 2008), at 1392

In determining the patentability under the machine-or-transformation test, the court states, at 1396: "The machine-or-transformation test is a two-branched inquiry; an applicant may show that a process claim satisfies §101 either by showing that his claim is tied to a particular machine, or by showing that his claim transforms an article."

Claims 74-84, 100-139 and 155-168 are clearly not tied to any particular machine. As to whether the claim performs a transformation of an article, while the claims makes reference as to how the fragments were generated (e.g. claim 74, step (a)), the claims themselves do not require the step of actually generating the fragments. This is clear from claims 85 and 140, which "further comprise" such steps. Hence, the transformation of an article (i.e. the target nucleic acid into fragments) found in claims 85 and 140 is lacking in claims 74-84, 100-139 and 155-168. Claims 76, 116 and 131,

Art Unit: 1637

which recite that the mass signals are determined by mass spectrometry, do not actually require *performing* mass spectrometry (merely using data produced therefrom), and so are not tied to a mass spectrometer (i.e. a machine). With regard to claims 112, 121, 127, 165, which further recite recording the results in a record, this is clearly the sort of "insignificant postsolution activity" discussed in *Bilski* ("The Diehr Court also reaffirmed a second corollary to the machine-or-transformation test by stating that 'insignificant postsolution activity will not transform an unpatentable principle into a patentable process.' ", at 1393).

As to whether the "mass signals" recited in claim 74 can be said to qualify as an article to be transformed, the *Bilski* court shed light on the issue in discussing *In re Abele and Marshall*, 214 USPQ 682 (C.C.P.A. 1982):

"In contrast, we held one of Abele's dependent claims to be drawn to patent-eligible subject matter where it specified that "said data is X-ray attenuation data produced in a two dimensional field by a computed tomography scanner." Abele, 684 F.2d at 908-09. This data clearly represented physical and tangible objects, namely the structure of bones, organs, and other body tissues. Thus, the transformation of that raw data into a particular visual depiction of a physical object on a display was sufficient to render that more narrowly-claimed process patent-eligible.

We further note for clarity that the electronic transformation of the data itself into a visual depiction in Abele was sufficient; the claim was not required to involve any transformation of the underlying physical object that the data represented. We believe this is faithful to the concern the Supreme Court articulated as the basis for the machine-or-transformation test, namely the prevention of pre-emption of fundamental principles. So long as the claimed process is limited to a practical application of a fundamental principle to transform specific data, and the claim is limited to a visual depiction that represents specific physical objects or substances, there is no danger that the scope of the claim would wholly pre-empt all uses of the principle." *In re Bilski*, 88 USPQ2d 1385 (Fed. Cir. 2008) at 1397, emphasis provided

In *Abele*, the X-ray data were "transformed" into an image; that is, the value of each data point was subjected to a subtraction of an average value of the data in the region surrounding that data point. Hence, the data point was "transformed" from one

Art Unit: 1637

value to a different value, and all of the modified data converted to an image. In the instant situation, the mass signals of the instant claims are not "transformed". The values of the mass signals in the instant claims are not converted or subtracted or otherwise modified in any manner. They are merely used to compile a list of all possible base compositions that would have such a mass. As a result of compiling such a list, the original mass signals are not altered in any way.

Therefore the claimed processes do not meet the machine-or-transformation test, affirmed in *Bilski* as "the governing test for determining patent eligibility of a process under § 101."

It is noted that Applicant could obviate this rejection in a number of ways, such as reciting an active step of performing mass spectrometry, thus tying the process to a particular machine, or alternatively incorporating the limitations of claims 85 or 140, thus reciting the actual physical transformation of an article (i.e. nucleic acid fragments). If the latter option is used, Applicant should be aware that claim 100 would still be subject to this rejection, since "simulated cleavage" would not actually transform any article. Claim 101 would not be subject to the rejection, since only the reference nucleic acid cleavage is simulated, whereas the target nucleic acids would be presumed to be *actually* cleaved.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

Art Unit: 1637

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 74-168 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 17-31, 42, 43 and 56-70 of copending Application No. 10/933,611. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the '611 application only differ from the instant claims in that they are more specific by way of reciting how the nucleic acid is prepared prior to base-specific fragmentation, mass spec analysis, identification of fragments that differ between the target and reference sequence, generation of compomer witnesses, and scoring sequence variation candidates. Thus the claims of the '611 application represent a species which anticipates the more generic claims of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

As Applicant has not filed a terminal disclaimer or argued the distinction between the instant claims and the claims of the '611 application, the double patenting rejection is maintained.

All other previous rejections have been withdrawn in view of Applicant's amendments. Applicant's arguments regarding the previous rejections have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL WOOLWINE whose telephone number is (571)272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1637

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Woolwine/
Examiner, Art Unit 1637